Remarks

I. The Outstanding Rejections

The Examiner maintained the rejection of claims 28-38, 43, 44, 47, and 48 under 35 U.S.C. § 103(a) for allegedly being obvious over U.S. Patent 4,792,447 ("the Uhr patent") in view of International Patent Publication WO 03/004056 ("the Raison publication") and Abe et al., *Am. J. Clin. Path.*, *100*, 67-74 (1993) ("the Abe article"). The Examiner also maintained the rejection of claims 39-42, 45, and 46 under 35 U.S.C. § 103(a) for allegedly being obvious in view of the Uhr patent in view of the Raison publication and the Abe article, and in further view of U.S. Patent Publication No. 2005/0255532 ("the Ruben publication").

II. The Rejections under 35 U.S.C. § 103(a) Should Be Withdrawn

In the Action, the Examiner indicates he considered the remarks in Applicants' previous response as well as the accompanying declaration by Dr. Jennings, but he maintains the Section 103 rejections. The Examiner refers to the decision in Ex Parte Erlich, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986) and asserts that whether an art is predictable or has a reasonable expectation of success is determined at the time the invention is made. In particular, the Examiner contends that the Jennings declaration refers to documents published after the priority date of the present application.

In response, Applicants respectfully submit that several of the publications referred to in the Jennings Declaration were published before the priority date of the present application. For example, Zimmer et al. (1990) and Dariavach et al. (1987) describe that the constant region of the kappa protein family is encoded by a single constant kappa gene, while there are at least four functional lambda constant genes; Kabat et al. (1975) was cited as describing the lack of sequence identity within the light chain constant domains; and Graille et al. (2001) was cited as evidence that a Peptostreptococcus mangus protein known to bind kappa light chains, did not bind lambda light chains, thus demonstrating it is not predictable whether a protein known to bind kappa light chain would bind lambda light chain

Further, Khurana et al. (2001) was cited as evidence that deposits of kappa and lambda light chains in different disease states take on different structures, again demonstrating the difference in structure of kappa and lambda light chains. Simon and Weiss

(1995) demonstrate further structural differences between these different protein families, with lambda light chains existing predominantly as dimers and kappa light chains mostly as monomers.

The only documents cited in the Jennings Declaration that were published after the priority date of the present application were James et al. (2007) and Bradwell (2008). These documents merely confirm the structural and functional differences between kappa and lambda light chains that had been described in the earlier evidentiary documents.

While the Examiner referred to section 2143.02 of the Manual of Patent Examining Procedure (MPEP), the original emphasis in this passage was not included. This section of the MPEP, including the original emphasis, recites that 'although an earlier case reversed a rejection because of unpredictability in the field of monoclonal antibodies, the court found "in this case at the time this invention was made, one of ordinary skill in the art would have been motivated to produce monoclonal antibodies specific for human fibroblast interferon using the method of [the prior art] with a reasonable expectation of success" 3 USPQ2d at 1016 (emphasis in original). Thus, it is clear from the emphasis applied to the above passage that the issues under consideration in Ex parte Erlich were specific to the particular factual circumstances relating to that patent application. The facts surrounding the present application can be distinguished from Ex parte Erlich.

In Ex parte Erlich [see also Ex parte Erlich and Nyari 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992)], the patent application in question related to monoclonal antibodies to human fibroblast interferon and was filed in 1981. The appellants argued non- obviousness in light of Kohler and Milstein (1975) on the basis that this prior art publication made it known that using hybridoma technology to produce monoclonal antibodies against water soluble antigens presented certain experimental barriers. The Examiner in that case, however, was able to refer to intervening prior art that was published between 1979 and 1980 (before the priority date) and which reported successful production of monoclonal antibodies using the hybridoma technology of Kohler and Milstein (1975), including production of antibodies to water soluble antigens. Thus, to whatever extent water soluble antigens presented difficulties when used in the Kohler and Milstein process in 1975, such difficulties were solved in 1980, a time just prior to the invention at issue.

Ex parte Erlich makes it clear, therefore, that prior art published around the time of or just prior to the invention should be considered when determining the predictability in the art. With regard to the present application, documents were cited in the Jennings Declaration which point to unpredictability in the art prior to the present invention. Unlike Ex parte Erlich, however, no intervening art has been cited that removes this unpredictability. Indeed, later publications confirm the structural differences between the kappa and lambda light chains.

The Examiner also asserts that both kappa and lambda light chains are structurally similar in their ability to form dimers with Ig heavy chain. However, the ability of kappa and lambda light chains to form dimers with Ig heavy chain is not relevant because the present claims are directed to antibodies that bind membrane associated lambda light chain in the absence of heavy chain.

The lack of structural similarity or known function of light chains in the absence of heavy chain meant that it could not have been predicted at the priority date of the present application that free lambda light chain would be expressed in the cell membrane of lymphoid cells. Thus, the claims are not rendered obvious in light of the Uhr patent when combined with the Raison publication and the Abe article, whether or not further combined with the Ruben publication. Accordingly, the rejection should be withdrawn.

For the reasons set forth above, the subject matter of claims 28-48 is patentable over the cited art, and the rejection under Section 103 should be withdrawn.

Conclusion

The application is in good and proper form for allowance, and Applicants respectfully request the Examiner to pass this application to issue.

This paper is accompanied by petition for a three-month extension of time with the required fee. The commissioner is authorized to charge any additional fees due in connection with this filing to Marshall, Gerstein and Borun, LLP deposit account number 13-2855, under order no. 29729/38914.

Dated: December 13, 2010

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